#15 JRP 10/28/99

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| Applicants: | Vere Hodge et al. | 21 October 1999 |
| Serial No.: | 08/945,249 | Group Art Unit No.: 1614 |
| Filed: | 2 February 1998 | Examiner: R. Travers |
| For: | Use of (R)-Penciclovir Triphosphate For the Manufacture of A Medicament For the Treatment of Viral Diseases | |

Assistant Commissioner of Patents
Washington, D.C. 20231

**RESPONSE**

Sir:

In response to the Examiner's Action mailed 5 January 1999, having a shortened statutory period of three(3) months, please enter the following Remarks and Amendments into the record. A Notice of Appeal accompanies this response.

**Remarks**

Claims 1, 3 to 14, and 16 to 20 are in the application. Applicants request clarification as to what the statement "Claims 1, 4, and 16 to 20 will be examined to the extent they read on the elected subject matter". The Examiner restricted the claims to method of use claims (1 and 4); Claims 3 and 8 to compositions; and claims 5 to 7 and 9 to compounds. Claims 1, 4 and 16 to 20 are all within the scope of the original restriction and should be examined in full.

Applicants gratefully acknowledge the withdrawal of the rejection to the claims under 35 USC §112 and 35 USC §102.

The claims presently stand rejected under 35 USC §103 as being unpatentable over Kenig et al. or Boyd et al., all of record. Applicants respectfully traverse this rejection.

Applicants reiterate that both the Kenig et al., and the Boyd et al. references do not disclose penciclovir triphosphate, nor do they disclose the (R)-isomer of this

compound. Both the Kenig et al. and the Boyd et al. patent application as are directed to different uses of Penciclovir. There is no teaching that phosphate esters of penciclovir could exist as enantiomers. There is no teaching of the specific bioprecurser phosphate esters claimed herein in claims 4, and 16 to 20.

It could not have been predicted that the (R) PCV-TP enantiomer would be a more active inhibitor of HBV DNA polymerases and HIV-1 reverse transcriptase than the (S)-enantiomer of PCV.

The Examiner has indicated that "Absent an illustration of unexpected benefits residing in one, or another, isomer these uses are obvious to the skilled artisan". As previously noted, the specification provides data supporting this unexpected activity on page 4, lines 14-22. The specification cites two references, copies of which have been forwarded to the Examiner, wherein PCV was found to exist in an enantiomeric form with the R isomer showing unexpected efficiency over the S isomer. Schinazi, R. is an author on one of these papers and a co-inventor of the present application. As this data is contained in the present application, which is signed by the inventors it is unclear what benefit would be gained by submission of this in declaration form. Applicants also submit herewith a PTOL 1449 form in order to clarify the record that these were in fact the two papers submitted with their 7 May 1999 response.

The Kenig et al., and Boyd et al. references do not provide a teaching, nor direction to direct the skilled artisan to synthesize specific phosphate esters of PCV, let alone (R) and (S) PCV-TP, in enantiomerically pure form. Kenig and Boyd et al. also do not provide a teaching nor direction for the specific use of these claimed phosphate esters of PCV (claims 1, 4 and 16 to 20) in the treatment of use with HIV-1 or HBV infections (page 4, lines 1 to 5 and Claim 1).

Specific methodology was necessarily developed to separate the two isomers described herein. The Kenig et al. or Boyd et al. references do not provide any motivation on how such a synthesis could be achieved.

There is no teaching, nor motivation in the Kenig et al. or Boyd et al. references to direct the skilled artisan to separate the isomers, nor that one of the isomers would posses the unexpected activity of being significantly more inhibitory against HIV-1 reverse transcriptase than the other. As the references do not provide such motivation, it is not seen that a prima facie case of obviousness has been made by the Examiner. The data supplied in the specification and abstracts is commensurate with the method of Claim 1 which is directed to the R enantiomer of PCV-TP.

In light these remarks, Applicants respectfully request reconsideration and withdrawal of the rejection to Claims 1, 4 and 16 to 20 under 35 USC §103.

**Conclusion**

Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. It is not believed that this paper should cause any additional fees or charges to be required, other than expressly provided for already. However, if this is not the case the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,

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